Editorial Commentary

Who are the real candidates for wedge resection of lung cancer?

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Zhang *et al.* (1) reported favorable outcomes for patients with invasive lung adenocarcinoma presenting as peripheral ground-glass nodules (GGNs) measuring ≤2 cm and a consolidation-to-tumor ratio (CTR) of ≤0.5 treated with wedge resection. On the other hand, the outcome of wedge resection was not tolerable in patients with GGNs measuring 2 to 3 cm and a CTR of ≤0.5 (1).

Several epoch-making findings regarding sublobar resection were recently published. Saji *et al.* (2) reported the benefits of segmentectomy versus lobectomy with respect to overall survival (OS) of patients with small peripheral non-small-cell lung cancer (NSCLC) with a tumor diameter of ≤2 cm and CTR of >0.5 (JCOG0802 trial). Altorki *et al.* (3,4) also reported the non-inferiority of sublobar resection, including both segmentectomy and wedge resection, versus lobectomy in terms of disease-free survival and OS of patients with NSCLC with a tumor diameter of ≤2 cm (CALGB140503 trial). Aokage *et al.* (5) reported favorable outcomes of segmentectomy for patients with GGNs measuring 2 to 3 cm and a CTR of ≤0.5 (JCOG1211 trial). These results defined segmentectomy as a standard procedure for patients with small peripheral NSCLC.

Regarding wedge resection, Suzuki *et al.* (6) reported remarkable outcomes of sublobar resection in patients with small peripheral NSCLC with a tumor diameter of ≤2 cm and CTR of ≤0.25; most of these procedures were wedge resections (JCOG0804 trial). In that study, 79% of patients underwent wedge resection (284 of 358 patients), and the 5-year relapse-free survival (RFS) rate for all patients was 99.7%. Although the authors did not compare the 5-year RFS rate between the wedge resection and segmentectomy groups, there were no differences in 5-year OS. In the current report by Zhang *et al.* (1), the 5-year RFS rate of patients with a tumor diameter of ≤2 cm and CTR of >0.25 to 0.5 was 96.89%. Although they performed a retrospective study and not a randomized prospective trial, their findings might suggest a new subset of patients that may benefit from wedge resection, (i.e., tumor diameter of ≤2 cm and CTR of >0.25 to 0.5).

However, an important concern of this report is the limited follow-up time, as the authors described. Ito *et al.* (7) performed a long-term (10-year) follow-up analysis of patients with clinical stage T1N0 cancer after lobectomy and reported that one patient with a tumor of ≤2 cm and CTR of >0.25 to 0.5 developed tumor recurrence after 5 years. This underscores the fact that a long follow-up period is warranted to reveal whether recurrence will develop in these tumors with lower malignancy. A longer follow-up period (10-year follow-up seems reasonable at this time) could reveal the real outcomes of the patients analyzed by Zhang *et al.* (1). Additionally, Li *et al.* (8) performed a 10-year follow-up analysis of patients with adenocarcinoma in situ (AIS) and minimally invasive adenocarcinoma (MIA) after wedge resection. Although there was no mention of

the CTR in their report, tumors with a diameter of ≤2 cm and CTR of ≤0.25 would theoretically be included as either pathological AIS or MIA, and there was no case of recurrence. At this time, tumors with a diameter of ≤2 cm and CTR of ≤0.25 are good candidates for wedge resection. With more concrete data, tumors with a diameter of ≤2 cm and CTR of >0.25 to 0.5 might also be included.

Another important issue of using the CTR as a selection criterion is the inconsistency of measurement. The CTR is sometimes difficult to measure because of the irregular shape of the lesion. It is also difficult to differentiate between a solid part and a GGN area with increased density. Rather than relying on subjective evaluations, we are awaiting an unbiased tool, such as artificial intelligence, that can perform uniform and objective evaluations.

The most important aspect of performing a wedge resection is the surgical margin. Both Zhang *et al.* (1) and Li *et al.* (8) required the margin to be >2 cm for tumors measuring ≤2 cm. The JCOG0804 trial reported by Suzuki *et al.* (6) required a 5-mm margin for tumors of ≤2 cm and a CTR of ≤0.25, and if the surgeon judged the margin to be insufficient, they converted the mode of surgery from wide wedge resection to segmentectomy or lobectomy. A narrow margin can readily lead to local recurrence. In the final report of the JCOG0804 at 10-year follow-up (9), despite efforts to secure adequate surgical margin by intraoperative inspection or frozen pathological examination, one local recurrence at the resection stump was observed at 8.3 years after wedge resection. Ensuring a precise surgical margin is required to obtain favorable results of wedge resection. Tumors with a low CTR are sometimes non-palpable; thus, several marking methods to localize the tumor and secure an adequate resection margin have been reported, such as computed tomography (CT)-guided lipiodol marking (10), virtual-assisted lung mapping (11), and a radiofrequency identification lung marking system (12). Segmentectomy is a valuable option for peripheral tumors that are expected to be non-palpable because of a low CTR or slightly deeper location and therefore might not require such a marking method. Wedge resection should be limited to tumor located peripherally, i.e., the outer one-third of the lung field like as JCOG0804 (6). Segmentectomy sometimes could be performed to tumor with slightly deeper location. For central tumor where the surgical margin is difficult to secure by segmentectomy, lobectomy should be chosen. To secure enough surgical margin more precisely, supportive methods such as above-mentioned preoperative marking or three-dimensional CT images would be useful as they are crucial for situating the lesion accurately within the lung parenchyma, even if the tumor is palpable.

Segmentectomy has several advantages over wedge resection. First, we can theoretically secure a more precise and adequate surgical margin because segmentectomy is a type of anatomical resection. That is, we can preoperatively plan a sufficient surgical margin by using high-resolution CT images. Development of imaging software using three-dimensional CT images would enable us to simulate the surgical procedure more easily (13). Second, anatomical resection enables us to resect GGNs that are non-palpable regardless of their depth. If the surgical resection is performed accurately according to the preoperative simulation, the tumor should theoretically be included in the resected specimen. Third, segmentectomy enables us to more easily resect interlobar or intersegmental lymph nodes, which are difficult to resect and evaluate during wedge resection. Segmentectomy is still an essential surgical procedure for such small peripheral tumors. However, if the surgical margin was insufficient due to the intraoperative factors such as misidentification or difficulty to identify the intersegmental plane, we always have to consider converting to lobectomy. It is also important to think about the difficulty and longer operating times associated with segmentectomy compared to wedge resection when choosing the adequate procedure.

The current report from Zhang *et al.* (1) demonstrates the possibility that small peripheral tumors with a diameter of ≤2 cm and CTR of ≤0.5 are candidates for wedge resection. Randomized controlled long-term trials compared wedge resection to segmentectomy for these groups could draw clear conclusion. However, segmentectomy is also an effective procedure for such tumors. As surgeons, we must always consider the adequacy of the surgical margins and select the surgical procedure accordingly.

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